CLEAN VERSION OF AMENDED CLAIMS:

1. (Amended) A method for expressing a heterologous gene in hepatocytes in culture comprising:

   - providing replication defective hepadnavirus particles at a titer level competent to infect hepatocytes, wherein the region of the pre-S or S-gene of the hepadnavirus genome has been replaced with the heterologous gene such that the expression of the heterologous gene is regulated by the regulatory sequences of the pre-S or the S-gene;

   - infecting hepatocytes with the hepadnavirus such that the heterologous gene is delivered into the hepatocytes and expressed in the hepatocytes, and wherein the replication defective hepadnavirus particles are one of human hepatitis B virus or duck hepatitis B virus particles

2. (Amended) The method of claim 42, wherein the replication defective hepadnavirus particles are human hepatitis B virus particles.

3. (Amended) The method of claim 42, wherein the heterologous gene replaces sequences of the S-gene.

4. (Amended) The method of claim 42, wherein the heterologous gene replaces a region of the S-gene under control of the endogenous S-promotor.

5. (Amended) The method of claim 42, wherein the heterologous gene is inserted such that one of an authentic AUG codon of the S-gene or [its] nucleotides encoding further amino acids of the S-protein are fused in frame to the 5' end of the heterologous gene.

6. (Amended) The method of claim 42, wherein the heterologous gene encodes a modulating agent.

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33. (Twice amended) A replication defective hepadnavirus particle of the group consisting of human hepatitis B virus and duck hepatitis B virus, wherein a region of a pre-S and S-gene of the hepadnavirus genome have been deleted and replaced by a heterologous gene such that the sequences for RC and RII that are essential for [producing] reverse [transcriptase] transcription are retained.

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37. (Twice Amended) A pharmaceutical composition comprising:

- a replication defective hepadnavirus of the group consisting of human hepatitis B virus and duck hepatitis B virus with a region of one of its pre-S-genes or S-genes deleted and replaced with a heterologous gene such that the sequences of the RC or RII that are essential for reverse transcription are retained, and
- a pharmaceutically acceptable carrier.

39. (Twice Amended) A method of producing replication defective hepadnavirus particles of human hepatitis B virus and duck hepatitis B virus at a titer suitable for infecting hepatocytes in culture comprising:

- co-transfecting hepatocyte cells of a hepatoma cell line with:

(i) replication defective hepadnavirus constructs, wherein a region of one of a pre S or an S-gene of the hepadnavirus DNA has been replaced with a gene encoding a heterologous gene while retaining one of an RC or RII signal, such that the expression of the gene encoding a cytokine is regulated by regulatory sequences of the S-gene; and

(ii) a helper construct for transcomplementing lacking viral gene products;

- culturing the hepatocytes until infectious viral particles are produced; and
- recovering the infectious particles.

41. (Amended) The method of claim 39, wherein the cell line is stably transfected with the helper construct and serves as a packaging cell line.

42. (Amended) A method for producing replication defective recombinant hepadnavirus particles capable of expressing a heterologous gene in hepatocytes in culture comprising:

- replacing an S-gene in a hepatitis B virus genome with the heterologous gene such that the expression of the heterologous gene is regulated by an S-promoter;
- producing a replication deficient hepadnavirus by means of a helper plasmid transcomplementing viral gene products such that the lacking viral gene products are present;
- Infecting hepatocytes with the recombinant hepadnavirus in culture, whereby the heterologous gene is delivered into the hepatocyte and expressed in the hepatocyte, wherein the replication defective recombinant hepadnavirus particles are human hepatitis B virus particles.

43. (Amended) A recombinant hepatitis B virus genome, wherein an S-gene in the genome is deleted and replaced by a heterologous gene and wherein the genome is selected from the group consisting of recombinant human hepatitis B virus or recombinant duck hepatitis B virus, and wherein the

sequences for RC and RII that are essential for reverse transcription are retained.

44. (Amended) The recombinant genome of claim 43, wherein the heterologeous gene is under the control of the endogenous S promoter.

45. (Amended) The recombinant genome of claim 43, wherein the heterologous gene is an immunomodulator.

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46. (Amended) The recombinant genome of claim 43, wherein the heterologous gene is a cytokine.

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47. (Amended) The recombinant genome of claim 44, wherein the immuno modulator is selected from the group consisting of IFNα, IFNβ, IFNγ, TNFα, IL-18 or IL-12.

48. (Amended) The recombinant genome of claim 43, wherein the heterologous gene is a chemokine.